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COMPARISON OF HEALTHCARE RESOURCE UTILIZATION, MEDICATION USE, AND COSTS AMONG HEART FAILURE PATIENTS WITH REDUCED AND PRESERVED EJECTION FRACTION

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Comparison of Healthcare Resource Utilization, Medication Use, and Costs among Heart Failure Patients with Reduced and Preserved Ejection Fraction

by

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Abstract

Comparison of Healthcare Resource Utilization, Medication Use, and Costs among Heart Failure Patients with Reduced and Preserved Ejection Fraction

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Objectives: To compare health care resource utilization, medication use, and associated costs among heart failure (HF) patients with reduced versus preserved ejection fraction (EF).

Methods: We included patients ≥ 18 years of age who had an inpatient admission with a primary discharge diagnosis of HF between October 1, 2011 and September 30, 2014 along with a recent EF measurement. Those with EF ≤ 40% were placed in the reduced EF group, and those with EF ≥ 50% were placed in the preserved EF group. Patients were excluded if they had an index length of stay (LOS) greater than 30 days, a prior heart transplant or LV atrial defibrillator. Baseline characteristics, healthcare utilization and associated costs, comorbidities, and medication use between the two groups were compared using inferential statistics and generalized linear models adjusted for clinical and demographic covariates were used to address the hypotheses, assessing the effect of EF group on utilization, costs, and medication use.

Results: A total of 380 HF patients were identified (54% female; mean [SD] age: 78.1 [12.0]), of which 116 (30%) had a reduced EF and 264 (69%) had a preserved EF. Those with preserved EF had a significantly greater proportion of females (60% vs 39%, p<0.001) and were older (mean [SD]: 79.0 [10.8] vs 76.0 [12.0] years, p=0.044). After adjusting for demographics, baseline utilization, and other clinical factors, EF group was not a significant predictor of any healthcare resource utilization or cost variable. Those with reduced EF had a higher prevalence of coronary heart disease (82% vs 62%, p<0.001) and cardiomyopathy (54% vs 15%, p<0.001) compared to those with preserved EF. Depression was more prevalent in HF patients with preserved EF (22% vs 11%, p=0.014) as compared to those with reduced EF. After controlling for demographics, baseline medication use, and other clinical characteristics, HF patients with reduced EF were shown to be less likely to have use of calcium channel blockers (OR: 0.380, 95% CI: 0.181-0.800, p=0.011).

Conclusion: This study demonstrated that healthcare utilization and associated costs are similar between HF patients with reduced and preserved EF, thus HF can be considered a single entity in terms of overall resource use. Findings also showed that HF patients with reduced EF have higher prevalence of coronary heart disease and cardiomyopathy, while having lower prevalence of depression. Those with reduced HF also had less use of calcium channel blockers.

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Chapter 1: Literature Review

Introduction

A progressive and chronic condition often punctuated by acute episodes, heart failure (HF) is a complex syndrome caused by structural or functional abnormality that impairs the ability of the ventricle to fill with or eject blood.[1] This impairment leads to reduced cardiac output, resulting in the cardinal clinical manifestations of HF: fatigue, shortness of breath, and often volume overload.[2] Due to these symptoms, HF patients often have reduced functional capacity, resulting in decreased quality of life and frequently leading to hospitalization.[3,4]

It was previously believed that reduced myocardial contractility, or systolic dysfunction, was the only disturbance in cardiac function responsible for HF; however, it is now known that a large proportion of patients with the HF syndrome have relatively normal systolic function. These patients have impairment of diastolic function due to slow left ventricular (LV) relaxation and increased stiffness.[5,6] Historically, such HF patients with normal LV ejection fraction (LVEF) were classified as having diastolic HF, and those with severe dilation and significantly reduced LVEF as having systolic HF. Diastolic HF was previously thought to account for about one-third of HF patients, and its prognosis was considered to be more benign than systolic HF, with lower mortality and morbidity rate.[7,8]

However, in the last decade, perspectives on how these syndromes are defined and their perceived burden have changed substantially. Because abnormalities of systolic and diastolic dysfunction can coexist in patients with HF, they are now characterized as HF with preserved EF (HFpEF) and HF with reduced EF (HFrEF). Also, in contrast to what was previously

known, recent studies have shown that prevalence of HF with preserved EF has increased to about half of patients with HF, with a prognosis similar to those with reduced EF.[6,9-11]

As described in greater detail in Table 1.1, a reduced EF is defined as ≤ 40%, while a preserved EF is defined as ≥ 50%.[12] EF is considered important in classification of HF because of differences in patient demographics, comorbid conditions, and response to treatment.[12,13] For example, HF patients with a preserved EF are more likely to be older and female compared to those with a reduced EF.[9,11,14] Also, compared to those with reduced EF, HF with preserved EF is associated with certain comorbidities, including hypertension, obesity, atrial fibrillation, diabetes, and anemia.[11,15] Because of these differences in demographic and clinical characteristics, a better understanding of how the burden of these two clinical entities differ will help clinicians better manage their HF patients, as well as inform decision making related to resource allocation.

Table 1.1 Definitions of HF with reduced and preserved EF[12]

Classification	EF (%)	Description
Heart failure with reduced ejection fraction (HFrEF)	≤ 40	– Also referred to as systolic HF. – Randomized controlled trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date.
Heart failure with preserved ejection fraction (HFpEF)	≥ 50	– Also referred to as diastolic HF. – Several different criteria have been used to further define HFpEF. – The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. – To date, efficacious therapies have not been identified.
HFpEF, borderline	41 to 49	– These patients fall into a borderline or intermediate group. – Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF
HFpEF, improved	> 40	– It has been recognized that a subset of patients with HFpEF previously had HFrEF. – These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. – Further research is needed to better characterize these patients.

EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Epidemiology

HF is a leading cause of death in the United States (US), with 1 in every 9 deaths having HF as a contributing cause in 2013.[4] With an estimated 5.7 million US adults currently affected by HF, projections show that the prevalence of HF will increase by almost 50% to over 8 million people by 2030.[3] Risk factors for developing HF include male gender, less education, physical inactivity, cigarette smoking, being overweight, diabetes, hypertension, valvular heart disease, and coronary heart disease.[16,17] In the well-known Framingham Heart Study sponsored by the National Heart, Lung, and Blood Institute (NHLBI), researchers found that there is a 20% lifetime risk of developing HF at 40 years of age.[18] It has also been shown that that the incidence of HF doubles with each 10-year increase in age after 65 years in men, with the incidence rate tripling for women after age 65.[19]

With HF being the most common hospital discharge diagnosis in patients over age 65, a large proportion of HF patients are elderly, having multiple comorbid conditions that influence morbidity and mortality.[4,20] Despite a decline in mortality rates over the last 50 years, the overall 5-year survival for HF patients is about 50%, with likelihood of death increasing with symptom severity.[20-22] Sudden cardiac death occurs in about 40% of patients, with serious ventricular arrhythmias often implicated as the underlying cause.[12,23] Evidence has shown that many factors (e.g., age, gender, EF, renal function, natriuretic peptide plasma concentrations, diabetes, extent of underlying coronary artery disease, blood pressure, HF etiology, and drug or device therapy) can affect the prognosis of HF patients.[21,24]

Among patients with HF, recent studies have estimated that approximately 47% to 55% have a preserved EF.[10,25-27] HF patients with preserved versus reduced ejection fraction have

distinct demographics and clinical characteristics. HF patients with a preserved EF are more likely to be older and female compared to those with reduced EF.[9,11,14] In addition, those with preserved EF tend to have greater prevalence of certain comorbidities, including hypertension, obesity, atrial fibrillation, diabetes, and anemia compared to those with reduced EF.[11,15] One study showed HF patients with a preserved EF had a higher risk of noncardiovascular death in comparison to those with reduced EF.[22] Despite these differences, however, overall prognosis of both HF syndromes are similar, with studies showing comparable mortality rates between the two groups.[9,15]

Disease Etiology and Pathogenesis

HF is a progressive disorder that is initiated after an event damages the cardiac muscle or impairs its ability to contract. This event can be abrupt, as in a myocardial infarction (MI), or gradual, as in chronic pressure or volume overload. Although the etiologies of HF with preserved versus reduced EF differ, there is still some overlap in the origins of these two conditions.[1,28] Common causes of HF are listed in Table 1.2.

The most common cause of both HF with reduced and preserved EF is coronary artery disease (CAD), with almost 70% of HF cases resulting from this.[15,29] CAD often leads to prolonged ischemia and eventually causes the irreversible death of myocardial cells, or MI. After an MI, the amount of cardiac muscle death affects the degree to which contractility is impaired. To maintain cardiac output, the body activates several compensatory mechanisms that allow patients to sustain LV function for a period of months to years, with patients remaining asymptomatic for some initial period of time.

Compensatory neurohormonal systems maintain cardiac output by retaining salt and water, and include the adrenergic nervous system, the renin-angiotensin-aldosterone system (RAAS), and the cytokine system.[1] These systems are the main target of current pharmacotherapies for HF with reduced EF. In addition, to increase myocardial contractility, the remaining functional cardiac muscle compensates by undergoing hypertrophic remodeling, which leads to further injury of the heart.[30]

In contrast to what is known about the pathogenesis of HF with reduced EF, the pathophysiology of HF with preserved EF is not well understood. Previously, diastolic dysfunction was considered to be the only mechanism responsible for the development of HF with preserved EF; however, a new paradigm suggests that non-cardiac mechanisms and comorbidities can drive myocardial dysfunction and remodeling in this disease.[25,31] This incomplete understanding of the pathophysiology of HF with preserved EF is the reason for the lack of effective therapies for this condition to date.

Table 1.2: Common Etiologies of Heart Failure[1]

Heart Failure with Reduced Ejection Fraction	Heart Failure with Preserved Ejection Fraction
Coronary artery disease	Pathologic hypertrophy
Myocardial infarction*	Primary (hypertrophic cardiomyopathies)
Myocardial ischemia*	Secondary (hypertension)
Chronic pressure overload	Aging
Hypertension*	Restrictive cardiomyopathy
Obstructive valvular disease*	Infiltrative disorders (amyloidosis, sarcoidosis)
Chronic volume overload	Storage diseases (hemochromatosis)
Regurgitant valvular disease	Fibrosis
Intracardiac (left-to-right) shunting	Endomyocardial disorders
Extracardiac shunting	
Chronic lung disease	
Cor pulmonale	
Pulmonary vascular disorders	
Nonischemic dilated cardiomyopathy	
Familial/genetic disorders	
Infiltrative disorders*	
Toxic/drug-induced damage	
Metabolic disorder*	
Viral	
Chagas' disease	
Disorders of rate and rhythm	
Chronic bradyarrhythmias	
Chronic tachyarrhythmias	

* Indicates conditions that can also lead to HF with preserved EF.
Adapted from Mann 2015.

Classification of Disease

The presence and severity of HF have been classified by the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA), as well as the New York Heart Association (NYHA).[23,32] The ACCF/AHA stages focus on development and worsening

of disease, which is reflective of the progressive nature of HF.[23] Patients in the ACCF/AHA HF Stages A and B are at risk for developing heart failure, whereas Stage C and D patients have confirmed HF.

The NYHA I-IV classification describes the patient's exercise capacity and the symptomatic disease severity using subjective evaluation by the clinician.[32] In contrast to the ACCF/AHA stages of HF, the NYHA classification does not assess disease progression, but rather severity of symptoms at a specific point in time. For example, the ACCF/AHA HF stage of a patient would not be able to improve from Stage C to Stage B, whereas the symptoms of the patient could fluctuate from NYHA class IV to I with diuretic therapy that improves volume overload. Both types of classifications are used together to guide evaluation and treatment of HF patients. Table 1.3 compares the differences between the two types of HF classification and demonstrates how they complement each other.

Table 1.3: Comparison of ACCF/AHA Stages of HF and NYHA Functional Classifications

ACCF/AHA Stages of HF[23]		NYHA Functional Classification[32]	
A	At high risk for HF but without structural heart disease or symptoms of HF	None	
B	Structural heart disease but without signs or symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
C	Structural heart disease with prior or current symptoms of HF	I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
		II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF
		III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF
		IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest
D	Refractory HF requiring specialized interventions	IV	Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

ACCF, American College of Cardiology Foundation; AHA, American Heart Association; HF, heart failure; and NYHA, New York Heart Association.

Clinical Guidelines for Management of Heart Failure

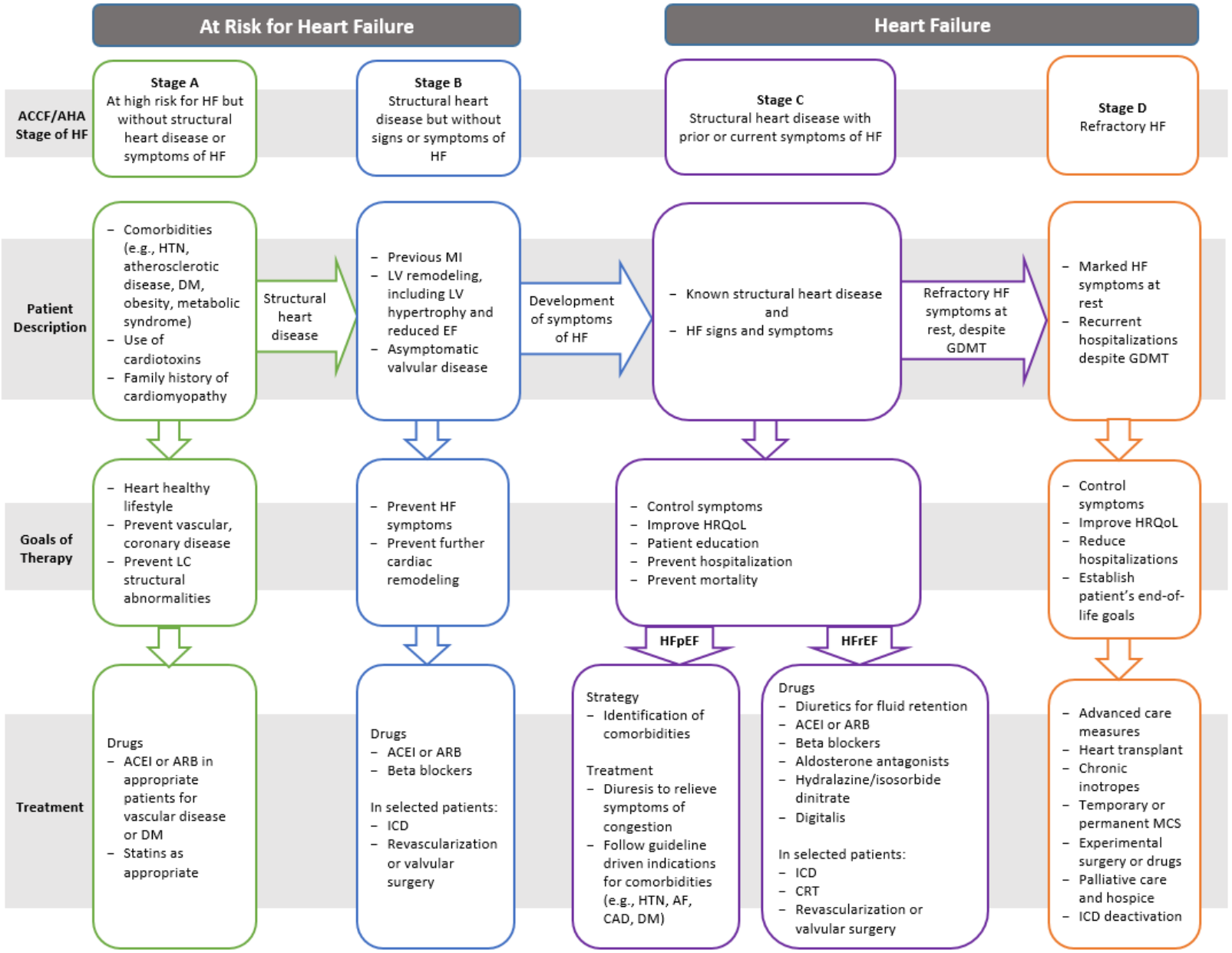
The ACCF and the AHA have collaborated to produce guidelines in the area of cardiovascular disease since 1980.[12] According to these guidelines, current treatment goals in

HF aim to improve both survival and health-related quality of life (HRQoL) of patients. Figure 1.1 depicts the evidence-based guideline-directed medical therapies recommended by the ACCF/AHA for each stage in the development of HF. For patients at risk for HF (Stages A and B), therapy focuses on treatment of HF risk factors, such as hypertension and diabetes. For Stage C, NYHA Class I-IV HFrEF, evidence-based therapies include an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), and a beta blocker. Depending on their NYHA classification and ethnicity, patients should also receive loop diuretics, hydral nitrates, or aldosterone antagonists as appropriate. For patients with EF < 35%, cardiac resynchronization therapy (CRT) or an implantable cardioverter-defibrillator (ICD) is recommended.[12]

In contrast to their efficacy in HF patients with reduced EF, the abovementioned drugs were found to have neutral outcomes in those with preserved EF.[33-41] As a result, guideline-directed medical therapy for HF with preserved EF focuses only on treatment of symptomatic congestion and comorbidities such as hypertension, atrial fibrillation, coronary artery disease, and diabetes mellitus.[12,42]

Patients with advanced, refractory HF (Stage D) have recurrent hospitalizations despite guideline-directed medical therapy. In these patients who are considered near the end of their life, treatments include advance care measures, such as heart transplant or mechanical circulatory support, followed by palliative care and hospice.

Figure 1.1: Stages in the development of HF and recommended therapy by ACCF/AHA stage[12]



ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; DM, diabetes mellitus; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HRQoL, health-related quality of life; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LV, left ventricular; MCS, mechanical circulatory support; and MI, myocardial infarction. Adapted from Yancy 2013.

Burden of Illness

Humanistic Burden

Due to their significantly reduced functional capacity, HF patients have poorer HRQoL as compared with the general population,[43] and even in comparison with patients suffering from other chronic diseases, such as chronic obstructive pulmonary disease, arthritis, diabetes, and other coronary diseases.[44-48] Factors that have been shown to have a negative influence on the HRQoL of patients with HF include disease severity and presence of comorbidities such as depression.[44,49,50] Other demographic factors that can impact HRQoL in patients with HF include age, gender, socioeconomic status, professional status, marital status, and the absence of a supportive social network.[43,44,51-53]

Although current treatment goals in heart failure are to improve both survival and HRQoL, recommended therapies that have survival benefits have only modest positive effect (e.g., ACEIs) or no impact (e.g., beta blockers) on HRQoL. In contrast, some therapies that have been shown to improve HRQoL, such as inotropic agents, do not improve survival.[54]

Economic Burden

In 2012, HF in the US was estimated to cost a total of $30.7 billion, 68% of which was attributed to direct medical costs. This estimate includes the cost of health care services, medications, and productivity. By the year 2030, total costs of HF are projected to increase to $69.7 billion, which is more than double the current cost of HF. The proportion related to direct medical costs is also expected to increase to over 75% of total medical costs, to $53 billion.[3] The greatest financial burden of treating chronic HF is attributed to hospitalizations, which costs between $12,000 to $31,000 per patient per hospitalization.[55]

A study comparing the 5-year medical costs between HF patients with reduced versus preserved EF found similar costs between the two groups ($49,128 vs $45,604), although HFrEF patients were found to have more cardiology encounters and cardiac procedures. In models accounting for comorbid conditions, the costs with normal and abnormal EF remained similar.[56]

Clinical Burden

Hospitalizations occur often after HF diagnosis, with about 83% of patients hospitalized at least once and 43% hospitalized at least 4 times.[57] Dunlay et al found that of these hospitalizations, more than half were unrelated to cardiovascular causes. Among Medicare beneficiaries, the overall HF hospitalization rate declined substantially in the last decade, but at a lower rate for African American men.[20] Data from the surveillance component of the Atherosclerosis Risk in Communities (ARIC) Study sponsored by the NHLBI found that in elderly patients (aged 55 years and older), the average incidence of HF hospitalization was 11.6 per 1000 patients per year. Of the incident hospitalized HF events, 53% had reduced EF and 47% had preserved EF. The ARIC study also found that among HF hospitalizations, African American men had the highest proportion of HF hospitalizations with reduced EF (70%), while Caucasian women had the highest proportion of HF hospitalization with preserved EF (59%).[58] After an HF hospitalization 1-year mortality was found to be about 30% and did not differ by race or sex.

A study in Olmsted County, MN showed that HF hospitalizations occurred more often among men and were similar in HF patients with reduced EF versus preserved EF. The study also found that, among those with HF, hospitalization rates for cardiovascular causes did not change over time, whereas those for noncardiovascular causes increased from 2000 to 2010.[22]

Study Objectives

In recent years, the differences between HF with reduced versus preserved LVEF have been better understood. However, to date, there have only been therapies proven to be efficacious in HF patients with reduced EF,[33-38] while there have been no trials that show improved outcomes for those with preserved EF.[34,36,39-41] Nonetheless, there are ongoing clinical trials for new therapies that have the potential to be safe and effective in patients with HF with preserved EF.[59] With the development of these novel and costly therapies targeting HF with preserved EF on the horizon, it is becoming important to understand the differences in burden of disease between those with reduced and preserved EF in order to make informed decisions related to resource allocation.

As demonstrated in the previously reviewed literature, HF with reduced versus preserved EF are distinct clinical entities with differing etiologies and demographic characteristics. For this reason, common outcomes of HF, such as hospitalization and other healthcare resource utilization may occur at different rates. However, comparative outcome studies have been inconclusive, and evidence comparing health care resource utilization and medication use are limited.[9,14,56,60-64] This study aims to compare health care resource utilization, medication use, and associated costs among HF patients with reduced versus preserved EF. Specific objectives and null hypotheses of this study include:

1. To determine whether healthcare resource utilization, including inpatient, emergency department, and outpatient visits, differs between HF patients with reduced versus preserved EF.

    $H_0$1.1: The difference in number of inpatient admissions between HF patients with reduced and preserved EF is not statistically significant.

$H_0$1.2: The difference in number of inpatient hospital days between HF patients with reduced and preserved EF is not statistically significant.

$H_0$1.3: The difference in number of primary care outpatient visits between HF patients with reduced and preserved EF is not statistically significant.

$H_0$1.4: The difference in number of cardiology outpatient visits between HF patients with reduced and preserved EF is not statistically significant.

$H_0$1.5: The difference in number of emergency department visits between HF patients with reduced and preserved EF is not statistically significant.

2. To determine whether healthcare costs, including prescription, inpatient, and outpatient costs, differ between HF patients with reduced versus preserved EF.

    $H_0$2.1: The difference in prescription costs between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$2.2: The difference in inpatient costs between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$2.3: The difference in outpatient costs between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$2.4: The difference in total overall costs between HF patients with reduced and preserved EF is not statistically significant.

3. To determine whether prevalence of comorbidities differ between HF patients with reduced versus preserved EF.

    $H_0$3.1: The difference in prevalence of diabetes between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$3.2: The difference in prevalence of dyslipidemia between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$3.3: The difference in prevalence of hypertension between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$3.4: The difference in prevalence of coronary heart disease between HF patients with reduced and preserved EF is not statistically significant.

    $H_0$3.5: The difference in prevalence of cardiomyopathy between HF patients with reduced and preserved EF is not statistically significant.

$H_0$3.6: The difference in prevalence of dysrhythmia between HF patients with reduced and preserved EF is not statistically significant.

$H_0$3.7: The difference in prevalence of valvular heart disease between HF patients with reduced and preserved EF is not statistically significant.

$H_0$3.8: The difference in prevalence of depression between HF patients with reduced and preserved EF is not statistically significant.

$H_0$3.9: The difference in prevalence of tobacco use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$3.10: The difference in prevalence of alcohol/other drug use between HF patients with reduced and preserved EF is not statistically significant.

4. To determine whether medication use differs between HF patients with reduced versus preserved EF.

$H_0$4.1: The difference in anticoagulant use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.2: The difference in antiarrhythmic use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.3: The difference in antilipemic use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.4: The difference in cardiotonic use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.5: The difference in beta-blocker use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.6: The difference in calcium channel blocker use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.7: The difference in use of RAAS-inhibiting agents between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.8: The difference in diuretic use between HF patients with reduced and preserved EF is not statistically significant.

$H_0$4.9: The difference in number of unique drugs between HF patients with reduced and preserved EF is not statistically significant.

Chapter 2: Methodology

Study Design and Data Source

This was a retrospective, observational review of claims and electronic medical record (EMR) data. Data were extracted from the Scott & White Health Plan (SWHP), which covers over 250,000 lives and is part of an integrated delivery network in Central Texas that includes a network of hospitals, clinics, and pharmacies. Pharmacy and medical claims, along with patient enrollment and medical care data containing demographic information, were linked longitudinally to EMR data. Pharmacy claims contain details from all dispensed prescriptions, including the drug name, date and quantity dispensed, days supplied, and plan- and patient-paid amounts. Medical claims provided detailed information on inpatient and outpatient services, including date and place of service, payments, procedure codes, and up to 5 International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis codes per date of care.

The date of admission of first hospitalization with a primary discharge diagnosis of HF was referred to as the index date. A recent EF measurement from an echocardiogram was used to determine the patient cohort. Data were collected from one year prior to the index date through 1 year post-admission including: details of index admission, and healthcare resource utilization and costs. Collected variables are described in greater detail in the following sections. This study was approved by the University of Texas at Austin and the Baylor Scott & White Health institutional review boards following expedited review.

Sample Selection

Patients at least 18 years of age with an inpatient admission with a primary discharge diagnosis of HF (ICD-9-CM 428.xx) between October 1, 2011 and September 30, 2014 were identified (fiscal years FY2012-FY2014). To be included in the study, patients had to be enrolled for 1 year prior to and at least 1 year after the index admission; the number of enrolled days was included as a covariate for patients with less than 2 full years of enrollment. In addition, patients were required to have a recent EF measurement from an echocardiogram to determine their placement into either EF group. Patients were excluded if they had an index length of stay (LOS) greater than 30 days, a prior heart transplant or LV atrial defibrillator.

Study Variables

The following baseline data parameters were collected from the one-year time period prior to the index admission: age, gender, costs of care (costs to patient; costs to health plan), medication use, and comorbidities. Comorbidities at baseline were identified using appropriate ICD-9-CM and Current Procedural Terminology (CPT) codes from medical claims, and American Hospital Formulary System (AHFS) codes from pharmacy claims, as described in Table 2.1. Variables related to the index admission included the length of stay and the most recent EF measurement from an echocardiogram, as well as the lag time between EF assessment and admission. Data parameters collected during the follow-up period after index admission included the number of inpatient admissions, hospital days, outpatient visits, emergency department visits, pharmacy dispenses, and costs (i.e., inpatient, outpatient, pharmacy, and total costs). Pharmacy utilization was normalized to a 30-day supply, and included the number

of unique medications overall, and number of dispenses of specific medication classes as described in Table 2.2.

Table 2.1: Diagnosis, Procedure, and Drug Codes used to Identify Comorbidities

Comorbidity	ICD-9-CM Codes	CPT or AHFS Codes
Coronary heart disease	410.x to 414.x	*Stent placement:* SG0291, C9600 to C6908; *Coronary bypass surgery:* S2205 to S2209
Diabetes mellitus	250.xx	
Hypertension	401.x to 405.x	*Anti-hypertensive drugs:* 242400, 242800, 243204, 243208, 402800, 402808, 402810, 402812, 402816, 402820, 402824
Depression	296.2 to 296.8, 300.4, 309.1, and 311	
Dyslipidemia	272.xx	
Valvular heart disease	424.0 to 424.3	
Cardiomyopathy	425.x	
Tobacco use disorder	305.1	
Cardiac dysrhythmias	427.x	

AHFS, American Hospital Formulary System; CPT, Current Procedural Terminology; ICD-9-CM, International Classification of Diseases, Ninth Edition, Clinical Modification

Table 2.2: AHFS Codes used to Identify Medication Classes

Drug Class	AHFS Code
Anti-arrhythmics	240404
Anti-hypertensives, renin-angiotensin-aldosterone system inhibitors	
Angiotensin II receptor antagonists	243208
Angiotensin-converting enzyme inhibitors	243204
Mineralocorticoid (aldosterone) antagonists	243220
Renin inhibitors	243240
Anti-hypertensives, other	
Hypotensive agents	240800
Central alpha-agonists	240816
Direct vasodilators	240820
Peripheral adrenergic inhibitors	240832
Anti-coagulants	201204
Calcium channel blockers	242800
Dihydropyridines	242808
Calcium-channel blocking agents, misc.	242892
Beta-blockers	242400
Cardiotonic agents (e.g. digoxin)	240408
Diuretics	402800
Loop diuretics	402808
Potassium-sparing diuretics	402810, 402816
Osmotic diuretics	402812
Thiazide diuretics	402820
Thiazide-like diuretics	402824
Anti-lipemics	240600
Antilipemic agents, miscellaneous	240692
HMG-CoA reductase inhibitors	240608
Fibric acid derivatives	240606
Cholesterol absorption inhibitors	240605
Bile acid sequestrants	240604

AHFS, American Hospital Formulary System

Statistical Analysis

Descriptive statistics for demographic characteristics, as well as for outcome variables were prepared. Continuous variables were reported as mean (standard deviation) or median (interquartile range) as appropriate, and categorical variables were reported as count (percentages). Baseline characteristics of HF patients with reduced versus preserved EF were compared using t-tests for continuous variables and chi-square tests for categorical variables. Generalized linear models weighted by months of eligibility and also adjusted for clinical and demographic covariates were used to address the hypotheses, assessing the effect of EF group on utilization, costs, and medication use. Outcomes included costs, count data on utilization and medication use, binary indicators of medication class use, and comorbidities.

Appropriate transformations were applied to the cost data, which are typically right-skewed and responsive to log-transform. Count data were analyzed by a Poisson model or related approach, depending on the distribution of the outcome, for example, negative binomial regression for over-dispersed data, the approach applied here based on the deviance factor. The binary outcomes were modeled by multivariable logistic regression. In the event the number of cases was too small to support all covariates, they were tested in a step-wise regression model to achieve a parsimonious adjusted model. All analyses were performed using SAS version 9.4, using the a priori alpha level of 0.05 for all statistical analyses.

In models regressing the HR-EF group on outcomes (utilization, costs, and medication use) adjusting for clinical and demographic covariates, an estimated regression coefficient associated with the HFrEF indicator whose 95% confidence interval excludes zero (or, 95% CI of OR [OR] or incident rate ratio [IRR] excludes 1) were supportive of the hypotheses.

Chapter 3: Results

Study Sample

A total of 831 patients with an HF admission were identified during the study period, 380 of which met all inclusion/exclusion criteria. Table 3.1 reports the sample attrition for the study.

Table 3.1: Sample Selection

Selection Criteria	n (%)
Inpatient admission with primary diagnosis of heart failure between Oct 1, 2010 and Sept 30, 2015	831 (100%)
Index admission between Oct 1, 2011 to Sept 30, 2014	601 (72%)
Index length of stay < 30 days	439 (53%)
No heart transplant or LV atrial defibrillator	439 (53%)
≥ 18 years old	438 (53%)
Ejection fraction ≤ 40 or ≥ 50	**380 (46%)**
Borderline ejection fraction (40 < EF < 50)	58 (7%)

Baseline Demographics and Clinical Characteristics

Table 3.2 provides demographics and clinical characteristics at baseline. Of the 380 HF patients meeting the selection criteria, 116 (31%) had a reduced EF and 264 (69%) had a preserved EF. Those with preserved EF had a significantly greater proportion of females (60% vs 39%, p<0.001) and were older (mean [SD]: 79.0 [10.8] vs 76.0 [14.2] years, p=0.044). Patients with reduced EF had a longer length of stay compared to those with preserved EF (mean [SD]: 7.2 [20.9] vs 4.1 [3.2] days, p=0.114), although the difference was not statistically significant.

By definition, those with reduced EF had lower mean LVEF compared to those with preserved EF (mean [SD]: 27.5 [8.8] vs 61.8 [8.0], p<0.001). Overall, only 56% of patients had an EF measurement within 1 month of the index admission, with the mean (SD) time between the most recent EF measurement and the index HF admission of 112.5 (149.6) or 3.8 (5.0) months.

Some differences in baseline comorbidities between the two groups were observed. HF patients with preserved EF had a greater prevalence of hypertension (89% vs 82%, p=0.045) compared to those with reduced EF. On the other hand, those with reduced EF had a higher prevalence of coronary heart disease (66% vs 50%, p=0.004) and cardiomyopathy (25% vs 7%, p<0.001) compared to those with preserved EF. Differences in prevalence of other comorbidities at baseline were not statistically significant.

Table 3.2: Baseline Demographics and Clinical Characteristics

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value*
Demographics				
Female, n	**204 (54)**	**45 (39)**	**159 (60)**	**<.001**
Age, years	**78.1 (12.0)**	**76.0 (14.2)**	**79.0 (10.8)**	**0.044**
Index variables				
Index admission length of stay, days	5.0 (11.9)	7.2 (20.9)	4.1 (3.2)	0.114
Left ventricular EF, %	**51.4 (17.8)**	**27.5 (8.8)**	**61.8 (8.0)**	**<.001**
Time between index admission and EF measurement**, days	112.5 (149.6)	100.7 (141.9)	117.6 (152.9)	0.145
EF within 1 year	305 (80%)	97 (84%)	208 (78%)	0.242
EF within 6 months	275 (72%)	90 (78%)	185 (70%)	0.114
EF within 3 months	242 (64%)	76 (66%)	166 (63%)	0.289
EF within 1 month	212 (56%)	67 (58%)	145 (55%)	0.303
Comorbidities, n (%)				
Diabetes	177 (47%)	52 (45%)	125 (47%)	0.650
Dyslipidemia	255 (67%)	77 (66%)	178 (67%)	0.842
Hypertension	**331 (87%)**	**95 (82%)**	**236 (89%)**	**0.045**
Coronary heart disease	**210 (55%)**	**77 (66%)**	**133 (50%)**	**0.004**
Cardiomyopathy	**47 (12%)**	**29 (25%)**	**18 (7%)**	**<0.001**
Dysrhythmia	226 (59%)	70 (60%)	156 (59%)	0.819
Valvular heart disease	80 (21%)	27 (23%)	53 (20%)	0.481
Depression	61 (16%)	16 (14%)	45 (17%)	0.426
Tobacco use	27 (7%)	6 (5%)	21 (8%)	0.331
Alcohol/other drug use	14 (4%)	5 (4%)	9 (3%)	0.668

Expressed as count (%) or mean (SD); EF, ejection fraction; HF, heart failure

*Bivariate analyses included t-tests for continuous data and chi-square tests for categorical data

**Truncated at 365 days

Healthcare Resource Utilization

Healthcare resource utilization at baseline is described in Table 3.3. Overall, 57% of HF patients had at least 1 inpatient admission at baseline, with 19% of patients having 5 or more admissions prior to the index event. Compared to those with preserved EF, those with reduced EF have greater inpatient hospital days (mean [SD]: 6.8 [13.8] vs 5.6 [10.4] days, p=0.925) and fewer outpatient primary care visits (mean [SD]: 10.8 [9.3] vs 13.5 [14.9] days, p=0.182) at baseline, although these differences were not statistically significant. HF patients with reduced EF were found to have significantly more cardiology visits at baseline compared to those with preserved EF (mean [SD]: 6.2 [8.3] vs 3.7 [5.1] days, p=0.006). Baseline inpatient admissions and emergency department visits were similar between the two groups.

A majority (94%) of patients overall had at least 1 re-hospitalization in the year following the index admission, with 25% having 5 or more hospitalizations. As shown in Table 3.4, unadjusted bivariate analysis revealed that HF patients with reduced EF had more outpatient visits to the cardiologist (mean [SD]: 7.9 [7.4] vs 5.8 [7.8] days, p<0.001), but fewer outpatient primary care visits (mean [SD]: 18.3 [16.6] vs 20 [14.3] days, p=0.040). However, after adjusting for demographic, baseline utilization, and other clinical factors, EF group was not a significant predictor of any healthcare resource utilization variable (Tables 3.5 to 3.9).

Table 3.3: Baseline Healthcare Resource Utilization

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value*
Covered days	349.7 (65.8)	352.3 (62)	348.6 (67.5)	0.618
At least 1 inpatient admission	218 (57%)	66 (57%)	152 (57%)	0.933
Number of inpatient admissions				
1	68 (18%)	19 (16%)	49 (18%)	
2	31 (8%)	8 (7%)	23 (9%)	
3	27 (7%)	7 (6%)	20 (8%)	0.745
4	18 (5%)	8 (7%)	10 (4%)	
More than 5	74 (19%)	24 (21%)	50 (19%)	
Inpatient admissions	2.5 (4.1)	2.5 (3.7)	2.5 (4.2)	0.860
Inpatient hospital days	6.0 (11.5)	6.8 (13.8)	5.6 (10.4)	0.925
Primary care visits	12.7 (13.5)	10.8 (9.3)	13.5 (14.9)	0.182
Cardiology visits	**4.5 (6.3)**	**6.2 (8.3)**	**3.7 (5.1)**	**0.006**
Emergency department visits	1.3 (2.0)	1.3 (1.9)	1.4 (2.0)	0.673

Expressed as mean (SD) or count (%); EF, ejection fraction; HF, heart failure
*Bivariate analyses included t-tests for continuous data, chi-square test for categorical data, and Wilcoxon rank-sum test for ordinal data

Table 3.4: Healthcare Resource Utilization during 1-year Follow-Up Period

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value*
Covered days	332.2 (92.2)	320.7 (101.9)	337.3 (87.4)	0.107
At least 1 inpatient admission	358 (94%)	107 (92%)	251 (95%)	0.351
Number of inpatient admissions				
1	105 (28%)	28 (24%)	77 (29%)	
2	76 (20%)	18 (16%)	58 (22%)	
3	41 (11%)	13 (11%)	28 (11%)	0.235
4	39 (10%)	13 (11%)	26 (10%)	
More than 5	97 (25%)	35 (30%)	62 (23%)	
Inpatient admissions	4.4 (6.5)	5.6 (9)	3.9 (5)	0.231
Inpatient hospital days	8.8 (15.8)	11.9 (21.6)	7.4 (12.2)	0.085
Primary care visits	**19.5 (15)**	**18.3 (16.6)**	**20 (14.3)**	**0.040**
Cardiology visits	**6.6 (7.7)**	**7.9 (7.4)**	**5.8 (7.8)**	**<0.001**
Emergency department visits	2.3 (2.5)	2.1 (2.3)	2.3 (2.6)	0.792

Expressed as mean (SD) or count (%); EF, ejection fraction; HF, heart failure
*Bivariate analyses included t-tests for continuous data, chi-square test for categorical data, and Wilcoxon rank-sum test for ordinal data

Table 3.5: Results of Negative Binomial Regression - Predicting Number of Inpatient Admissions by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	0.211	3.310	1.235	0.984	1.549	0.069
Inpatient admissions at baseline	**0.079**	**31.280**	**1.083**	**1.053**	**1.113**	**<0.001**
Lag between EF and admission	0.000	0.340	1.000	1.000	1.001	0.560
Covered days	0.000	0.080	1.000	0.999	1.002	0.776
Female	-0.125	1.310	0.883	0.713	1.093	0.252
Age	**-0.023**	**25.540**	**0.977**	**0.968**	**0.986**	**<0.001**

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.6: Results of Negative Binomial Regression - Predicting Inpatient Hospital Days by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	0.254	3.120	1.289	0.972	1.709	0.078
Inpatient hospital days at baseline	**0.032**	**18.420**	**1.033**	**1.018**	**1.048**	**<0.001**
Lag between EF and admission	0.000	0.100	1.000	0.999	1.001	0.748
Covered days	0.001	1.630	1.001	0.999	1.003	0.202
Female	-0.150	1.280	0.861	0.664	1.116	0.259
Age	**-0.031**	**28.360**	**0.969**	**0.958**	**0.981**	**<0.001**

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.7: Results of Negative Binomial Regression - Predicting Primary Care Visits by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	-0.088	1.110	0.916	0.778	1.078	0.291
Primary care visits at baseline	**0.012**	**12.750**	**1.012**	**1.005**	**1.018**	**<0.001**
Lag between EF and admission	**-0.001**	**4.020**	**1.000**	**0.999**	**1.000**	**0.045**
Covered days	0.000	0.010	1.000	0.999	1.001	0.924
Female	-0.025	0.110	0.975	0.839	1.134	0.745
Age	-0.007	3.550	0.993	0.986	1.000	0.059

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.8: Results of Negative Binomial Regression - Predicting Cardiology Visits by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	0.163	2.340	1.177	0.955	1.451	0.126
Cardiology visits at baseline	**0.039**	**19.330**	**1.040**	**1.022**	**1.058**	**<0.001**
Lag between EF and admission	**-0.001**	**4.000**	**0.999**	**0.999**	**1.000**	**0.046**
Covered days	0.001	2.360	1.001	1.000	1.003	0.124
Female	-0.188	3.510	0.829	0.681	1.009	0.061
Age	**-0.017**	**14.190**	**0.983**	**0.974**	**0.992**	**<0.001**

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.9: Results of Negative Binomial Regression - Predicting Number of Emergency Department Visits by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	-0.035	0.090	0.966	0.774	1.206	0.759
Emergency department visits at baseline	**0.171**	**50.110**	**1.186**	**1.132**	**1.244**	**<0.001**
Lag between EF and admission	0.000	0.070	1.000	0.999	1.001	0.798
Covered days	0.000	0.320	1.000	0.998	1.001	0.574
Female	0.030	0.080	1.030	0.838	1.266	0.778
Age	-0.006	1.710	0.994	0.985	1.003	0.190

CI, confidence interval; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Costs

Baseline inpatient costs (total, plan and patient costs) were significantly higher in those with reduced EF (mean [SD] total inpatient costs: $3,047 [$14,467] vs $1,648 [$8,014], p=0.042; plan paid inpatient costs: $2,833 [$14,114] vs $1,583 [$7,926], p=0.048; patient paid inpatient costs: $214 [$665] vs $65 [$266], p=0.048; Table 3.10). Other healthcare costs were similar between the two groups during the 1-year period prior to index admission (Table 3.11).

Unadjusted analysis found that those with reduced EF had greater overall costs on average (mean [SD]: $23,782 [$101,155] vs $7,695 [$13,568], p=0.888; Table 3.12). However, after controlling for demographics and baseline costs, EF group was not found to be a significant predictor of any follow-up cost variables (Tables 3.13 to 3.165).

Table 3.10: Baseline Healthcare Costs

Mean (SD), $ Median [IQR], $	**All (N=380)**	**HF with Reduced EF (n=116)**	**HF with Preserved EF (n=264)**	**p-value***
Total Overall Costs	7,654 (15,530) 4,313 [6,180]	8,951 (19,602) 4,503 [7,131]	7,084 (13,359) 4,281 [5,821]	0.351
Total Inpatient Costs	**2,075 (10,416) 0 [1,566]**	**3,047 (14,467) 0 [1,844]**	**1,648 (8,014) 0 [990]**	**0.042**
Costs to Health Plan	**1,965 (10,216) 0 [1,208]**	**2,833 (14,114) 0 [1,678]**	**1,583 (7,926) 0 [746]**	**0.048**
Costs to Patient	**111 (433) 0 [0]**	**214 (665) 0 [0]**	**65 (266) 0 [0]**	**0.014**
Total Outpatient Costs	3,758 (8,045) 1,934 [3,025]	4,434 (10,666) 1,958 [3,669]	3,462 (6,575) 1,911 [2,902]	0.926
Costs to Health Plan	3,482 (7,691) 1,786 [2,871]	4,116 (10,305) 1,734 [3,178]	3,204 (6,210) 1,793 [2,688]	0.987
Costs to Patient	276 (642) 45 [244]	318 (674) 67 [289]	257 (628) 35 [228]	0.218
Total Pharmacy Costs	1,820 (2,340) 925 [2,662]	1,470 (2,202) 670 [1,992]	1,974 (2,385) 1,073 [2,924]	0.215
Costs to Health Plan	1,400 (1,990) 572 [2,107]	1,084 (1,869) 424 [1,419]	1,539 (2,029) 763 [2,473]	0.108
Costs to Patient	420 (592) 205 [584]	386 (587) 163 [486]	435 (594) 219 [611]	0.880

EF, ejection fraction; HF, heart failure; IQR, interquartile range; SD, standard deviation

*Bivariate analyses included t-tests for continuous data

Table 3.11: Healthcare Costs During 1-Year Follow-Up

Mean (SD), $ Median [IQR], $	**All (N=380)**	**HF with Reduced EF (n=116)**	**HF with Preserved EF (n=264)**	**p-value***
Total Overall Costs	12,606 (57,337) 4,612 [7,167]	23,782 (101,155) 3,684 [7,986]	7,695 (13,568) 4,759 [6,604]	0.888
Total Inpatient Costs	6,919 (52,342) 0 [1,943]	16,913 (92,612) 0 [2,122]	2,528 (11,586) 0 [1,794]	0.102
Costs to Health Plan	3,122 (7,953) 1,548 [3,010]	4,183 (13,378) 1,486 [2,875]	2,656 (3,491) 1,602 [3,126]	0.379
Costs to Patient	236 (668) 30 [190]	280 (595) 68 [253]	216 (698) 22 [162]	0.196
Total Outpatient Costs	3,358 (8,196) 1,723 [3,256]	4,462 (13,632) 1,651 [3,061]	2,873 (3,843) 1,740 [3,325]	0.423
Costs to Health Plan	1,843 (5,087) 608 [2,337]	1,979 (7,493) 303 [1,319]	1,783 (3,569) 797 [2,488]	0.113
Costs to Patient	486 (822) 218 [648]	427 (858) 202 [483]	511 (807) 233 [704]	0.770
Total Pharmacy Costs	2,328 (5,672) 907 [2,832]	2,406 (8,075) 511 [1,894]	2,294 (4,225) 1,130 [3,239]	0.225
Costs to Health Plan	6,753 (52,113) 0 [1,742]	16,667 (92,313) 0 [2,013]	2,397 (11,175) 0 [1,635]	0.116
Costs to Patient	166 (658) 0 [0]	246 (694) 0 [0]	131 (639) 0 [0]	0.052

EF, ejection fraction; HF, heart failure; IQR, interquartile range; SD, standard deviation

*Bivariate analyses included t-tests for continuous data

Table 3.12: Results of Linear Regression: Predicting Total Overall Costs by Demographic and Clinical Variables

Variable (Reference Group)	Estimate	Standard Error	t-value	p-value
HFrEF (HFpEF)	0.097	0.176	0.550	0.582
Log of baseline total overall costs	**0.896**	**0.036**	**24.670**	**<0.001**
Lag between EF and admission	-0.001	0.001	-1.530	0.128
Covered days	-0.002	0.001	-1.800	0.072
Female (Male)	0.302	0.164	1.840	0.067
Age	**-0.025**	**0.007**	**-3.690**	**<0.001**

CI, confidence interval; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.13: Results of Linear Regression: Predicting Inpatient Costs by Demographic and Clinical Variables

Variable (Reference Group)	Estimate	Standard Error	t-value	p-value
HFrEF (HFpEF)	0.443	0.445	1.000	0.320
Log of baseline inpatient costs	**0.484**	**0.051**	**9.540**	**<0.001**
Lag between EF and admission	0.002	0.001	1.170	0.243
Covered days	0.002	0.003	0.730	0.464
Female (Male)	0.467	0.414	1.130	0.260
Age	-0.009	0.017	-0.550	0.583

CI, confidence interval; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.14: Results of Linear Regression: Predicting Outpatient Costs by Demographic and Clinical Variables

Variable (Reference Group)	Estimate	Standard Error	t-value	p-value
HFrEF (HFpEF)	-0.281	0.220	-1.270	0.203
Log of baseline outpatient costs	**0.751**	**0.044**	**17.150**	**<0.001**
Lag between EF and admission	**-0.001**	**0.001**	**-2.220**	**0.027**
Covered days	-0.001	0.002	-0.600	0.550
Female (Male)	0.295	0.206	1.430	0.153
Age	**-0.029**	**0.009**	**-3.390**	**0.001**

EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.15: Results of Linear Regression: Predicting Pharmacy Costs by Demographic and Clinical Variables

Variable (Reference Group)	Estimate	Standard Error	t-value	p-value
HFrEF (HFpEF)	-0.136	0.237	-0.570	0.567
Log of baseline pharmacy costs	**0.873**	**0.031**	**27.830**	**<0.001**
Lag between EF and admission	-0.001	0.001	-1.400	0.161
Covered days	-0.001	0.002	-0.840	0.400
Female (Male)	0.159	0.223	0.710	0.477
Age	**-0.026**	**0.009**	**-2.870**	**0.004**

EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Comorbid Conditions

Table 3.16 compares comorbidities between the two groups during the follow up period. Following the baseline trend, those with reduced EF had a higher prevalence of coronary heart disease (82% vs 62%, p<0.001) and cardiomyopathy (54% vs 15%, p<0.001) compared to those with preserved EF. Depression was more prevalent in HF patients with preserved EF (22% vs 11%, p=0.014) as compared to those with reduced EF. Differences in prevalence of other comorbidities of interest were not statistically significant.

Table 3.16: Comorbid Conditions During 1-Year Follow Up

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value
Diabetes	171 (45%)	48 (41%)	123 (47%)	0.347
Dyslipidemia	253 (67%)	78 (67%)	175 (66%)	0.856
Hypertension	349 (92%)	103 (89%)	246 (93%)	0.150
Coronary heart disease	**259 (68%)**	**95 (82%)**	**164 (62%)**	**<0.001**
Cardiomyopathy	**101 (27%)**	**63 (54%)**	**38 (14%)**	**<0.001**
Dysrhythmia	287 (76%)	90 (78%)	197 (75%)	0.536
Valvular heart disease	125 (33%)	44 (38%)	81 (31%)	0.166
Depression	**71 (19%)**	**13 (11%)**	**58 (22%)**	**0.013**
Tobacco use	31 (8%)	9 (8%)	22 (8%)	0.851
Alcohol/other drug use	13 (3%)	3 (3%)	10 (4%)	0.553

Expressed as count (%); EF, ejection fraction; HF, heart failure
*Unadjusted bivariate analyses included chi-square tests for categorical data

Medication Use

As shown in Table 3.17, the reduced EF group had a greater proportion of patients with antiarrhythmic use (16% vs 8%, p=0.035), but fewer patients with calcium-channel blocker use (19% vs 37%, p=0.001) at baseline. The proportion of patients using other medications of interest at baseline was similar between the two groups. The number of unique medications used by each group was also similar (mean [SD]: 9.4 [8.1] vs 10.3 [8.1], p=0.145).

Among those on a medication, unadjusted bivariate analysis revealed that those with preserved EF have a greater number of antiarrhythmic (mean [SD] 30-day fills: 7.2 [3.4] vs 4.0 [3.7], p=0.003) and antilipemic (mean [SD] 30-day fills: 9.1 [3.3] vs 6.9 [4], p=0.001) prescriptions during 1-year follow-up (Table 3.18). A greater proportion of those with preserved EF had calcium channel blocker use (30% vs 11%, p<0.001). After controlling for demographics, baseline medication use, and other clinical characteristics, logistic regression revealed that HF patients with reduced EF were less likely to have use of calcium channel blockers (Table 3.20; OR: 0.380, 95% CI: 0.181-0.800, p=0.011). EF group was not a significant predictor of medication use in any of the other drug classes of interest (Tables 3.21 to 3.29).

Table 3.17: Medication Use at Baseline by Drug

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value*
Number of unique medications, mean (SD)	10.0 (8.1)	9.4 (8.1)	10.3 (8.1)	0.145
Medication Use				
Anticoagulants	85 (22)	23 (20)	62 (23)	0.441
Antiarrhythmics	**40 (10)**	**18 (16)**	**22 (8)**	**0.035**
Antilipemics	179 (47)	51 (44)	128 (48)	0.435
Cardiotonics	37 (10)	15 (13)	22 (8)	0.160
Beta-blockers	211 (55)	63 (54)	148 (56)	0.781
Calcium channel blockers	**119 (31)**	**22 (19)**	**97 (37)**	**0.001**
RAAS-inhibiting agents	193 (51)	62 (53)	131 (49)	0.471
Other antihypertensives	32 (8)	5 (4)	27 (10)	0.057
Diuretics	55 (14)	17 (14)	39 (15)	0.834

Expressed as count of patients on a medication (%), unless otherwise specified; EF, ejection fraction; HF, heart failure; RAAS, renin-angiotensin-aldosterone system

*Bivariate analyses included t-tests for continuous data and chi-square tests for categorical data

Table 3.18: Medication Use during 1-Year Follow Up

	All (N=380)	HF with Reduced EF (n=116)	HF with Preserved EF (n=264)	p-value*
Anticoagulants	87 (23)	25 (22)	62 (23)	0.693
Antiarrhythmics	44 (12)	19 (16)	25 (9)	0.051
Antilipemics	173 (45)	46 (40)	127 (48)	0.136
Cardiotonics	44 (12)	17 (15)	27 (10)	0.209
Beta-blockers	221 (58)	64 (55)	157 (59)	0.459
Calcium channel blockers	**93 (24)**	**13 (11)**	**80 (30)**	**<0.001**
RAAS-inhibiting agents	214 (56)	67 (58)	147 (55)	0.679
Other antihypertensives	40 (10)	9 (8)	31 (12)	0.248
Diuretics	245 (64)	77 (66)	168 (63)	0.576

Expressed as count of patients on a medication (%); EF, ejection fraction; HF, heart failure; RAAS, renin-angiotensin-aldosterone system

*Bivariate analyses included chi-square tests for categorical data

Table 3.19: Baseline Number of Prescriptions Among Patients on a Medication

	All (N=380)	HF with Reduced EF	HF with Preserved EF	p-value*
Anticoagulants	6.9 (4.1)	7 (4.2)	6.8 (4)	0.690
Antiarrhythmics	7 (4.1)	6 (4.3)	7.7 (3.9)	0.248
Antilipemics	**9 (3.4)**	**8.1 (3.7)**	**9.3 (3.3)**	**0.017**
Cardiotonics	7.9 (3.9)	7 (4)	8.6 (3.8)	0.398
Beta-blockers	8.9 (3.7)	8.4 (3.8)	9.1 (3.7)	0.093
Calcium channel blockers	8.6 (3.7)	7.3 (3.9)	8.9 (3.6)	0.090
RAAS-inhibiting agents	8.7 (3.7)	8.4 (3.6)	8.8 (3.7)	0.343
Other antihypertensives	5.8 (4)	3.8 (4.8)	6.2 (3.8)	0.166
Diuretics	7.8 (3.8)	7.3 (3.8)	8 (3.8)	0.211

Expressed as mean number of 30-day fills (SD); EF, ejection fraction; HF, heart failure; RAAS, renin-angiotensin-aldosterone system

*Bivariate analyses included Kruskal-Wallis tests for ordinal data.

Table 3.20: Number of Prescriptions Among Patients on a Medication during 1-year Follow-Up

	All (N=380)	HF with Reduced EF	HF with Preserved EF	p-value*
Anticoagulants	7.5 (3.9)	7.9 (3.8)	7.4 (3.9)	0.612
Antiarrhythmics	**5.8 (3.8)**	**4 (3.7)**	**7.2 (3.4)**	**0.003**
Antilipemics	**8.5 (3.6)**	**6.9 (4)**	**9.1 (3.3)**	**0.001**
Cardiotonics	6.8 (4)	5.8 (3.9)	7.3 (4)	0.216
Beta-blockers	7.9 (3.7)	7.6 (3.6)	8 (3.7)	0.300
Calcium channel blockers	6.7 (4.1)	5.5 (4.4)	6.8 (4.1)	0.191
RAAS-inhibiting agents	8 (4)	8 (4)	8 (4)	0.974
Other antihypertensives	6 (4.2)	6 (3.2)	6 (4.4)	0.832
Diuretics	7.6 (4)	7 (4.2)	7.8 (3.8)	0.208

Expressed as mean number of 30-day fills (SD); EF, ejection fraction; HF, heart failure; RAAS, renin-angiotensin-aldosterone system

*Bivariate analyses included Kruskal-Wallis tests for ordinal data

Table 3.21: Results of Logistic Regression - Predicting Number of Unique Medications by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Incident Rate Ratio (IRR)	95% CI of IRR		p-value
				Lower	Higher	
HFrEF	0.051	0.700	1.052	0.935	1.184	0.402
Unique medications at baseline	**0.115**	**584.060**	**1.122**	**1.111**	**1.132**	**<0.001**
Lag between EF and admission	0.000	0.310	1.000	1.000	1.000	0.579
Covered days	0.000	0.200	1.000	0.999	1.001	0.653
Female	-0.001	0.000	0.999	0.897	1.113	0.990
Age	0.003	1.950	1.003	0.999	1.008	0.162

CI, confidence interval; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.22: Results of Logistic Regression - Predicting Anticoagulant Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	0.068	3.499	1.070	0.549	2.088	0.842
Anticoagulant use at baseline	**3.067**	**0.040**	**21.483**	**11.626**	**39.699**	**<0.001**
Lag between EF and admission	0.000	95.853	1.000	0.999	1.000	0.550
Covered days	0.000	0.357	1.000	0.999	1.000	0.722
Female	0.215	0.127	1.240	0.669	2.298	0.494
Age	-0.002	0.467	0.998	0.971	1.025	0.862

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.23: Results of Logistic Regression - Predicting Antiarrhythmic Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	0.085	0.034	1.088	0.444	2.666	0.853
Antiarrhythmic use at baseline	**4.030**	**71.815**	**56.232**	**22.144**	**142.798**	**<0.001**
Lag between EF and admission	-0.001	1.096	0.999	0.998	1.000	0.295
Covered days	0.000	1.027	1.000	0.999	1.000	0.311
Female	-0.448	0.979	0.639	0.263	1.552	0.322
Age	-0.023	1.893	0.977	0.946	1.010	0.169

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.24: Results of Logistic Regression - Predicting Antilipemic Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	-0.626	3.115	0.535	0.267	1.072	0.078
Antilipemic use at baseline	**4.074**	**144.264**	**58.766**	**30.230**	**114.238**	**<0.001**
Lag between EF and admission	-0.001	3.384	0.999	0.999	1.000	0.066
Covered days	-0.001	2.930	1.000	0.999	1.000	0.087
Female	-0.160	0.233	0.852	0.445	1.631	0.629
Age	-0.021	2.464	0.980	0.955	1.005	0.117

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.25: Results of Logistic Regression - Predicting Cardiotonic Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	0.365	0.675	1.441	0.603	3.445	0.411
Cardiotonic use at baseline	**3.747**	**71.852**	**42.378**	**17.820**	**100.781**	**<0.001**
Lag between EF and admission	0.000	0.410	1.000	0.999	1.001	0.522
Covered days	0.000	0.017	1.000	0.999	1.001	0.897
Female	0.217	0.249	1.242	0.530	2.910	0.618
Age	0.006	0.128	1.007	0.971	1.043	0.720

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.26: Results of Logistic Regression - Predicting Beta Blocker Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	-0.138	0.251	0.871	0.508	1.493	0.616
Beta blocker use at baseline	**2.521**	**94.919**	**12.439**	**7.491**	**20.655**	**<0.001**
Lag between EF and admission	0.000	0.004	1.000	0.999	1.001	0.950
Covered days	0.000	2.940	1.000	0.999	1.000	0.086
Female	**0.523**	**4.036**	**1.687**	**1.013**	**2.808**	**0.045**
Age	-0.018	2.953	0.982	0.962	1.003	0.086

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.27: Results of Logistic Regression - Predicting Calcium Channel Blocker Use by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	**-0.966**	**6.493**	**0.380**	**0.181**	**0.800**	**0.011**
Calcium channel blocker use at baseline	**2.826**	**78.914**	**16.877**	**9.047**	**31.484**	**<0.001**
Lag between EF and admission	0.000	1.593	1.000	0.999	1.000	0.207
Covered days	0.000	0.966	1.000	0.999	1.000	0.326
Female	0.452	1.882	1.572	0.824	3.001	0.170
Age	-0.023	3.165	0.977	0.953	1.002	0.075

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Table 3.28: Results of Logistic Regression - Predicting Use of RAAS-inhibiting Agents by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	0.045	0.029	1.046	0.620	1.763	0.866
RAAS-inhibiting agent use at baseline	**2.129**	**77.323**	**8.404**	**5.229**	**13.506**	**<0.001**
Lag between EF and admission	0.000	1.169	1.000	0.999	1.000	0.280
Covered days	0.000	0.673	1.000	1.000	1.001	0.412
Female	0.390	2.460	1.477	0.907	2.403	0.117
Age	-0.019	3.545	0.981	0.962	1.001	0.060

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction; RAAS, renin-angiotensin-aldosterone system

Table 3.29: Results of Logistic Regression - Predicting Use of Diuretics by Demographic and Clinical Variables

	Estimate	Wald Chi-Square	Odds Ratio	95% CI of Odds Ratio		p-value
				Lower	Higher	
HFrEF	0.254	0.852	1.289	0.752	2.208	0.356
Diuretic use at baseline	**2.131**	**71.874**	**8.424**	**5.147**	**13.787**	**<0.001**
Lag between EF and admission	0.000	0.415	1.000	0.999	1.000	0.520
Covered days	0.000	2.868	1.000	1.000	1.001	0.090
Female	0.424	2.773	1.529	0.928	2.519	0.096
Age	-0.013	1.708	0.987	0.967	1.007	0.191

CI, confidence interval; EF, ejection fraction; and HFrEF, heart failure with reduced ejection fraction

Summary of Results

Results for all hypotheses tested are reported in Table 3.30. Healthcare resource utilization (Objective 1) and associated costs (Objective 2) were not found to be statistically different compared between those with reduced and preserved EF. Those with reduced EF have higher prevalence of coronary heart disease and cardiomyopathy (Objective 3), and less calcium channel blocker use (Objective 4).

Table 3.30: Results of Hypotheses Testing

Objectives and Alternate Hypotheses (H_1)	**Result**
Objective 1 To determine whether healthcare resource utilization differs between HF patients with reduced and preserved EF.	
$H_1$1.1: The number of inpatient admissions of HF patients with reduced EF is greater than that of those with preserved EF.	Rejected
$H_1$1.2: The number of inpatient hospital days of HF patients with reduced EF is greater than that of those with preserved EF.	Rejected
$H_1$1.3: The number of primary care outpatient visits of HF patients with reduced EF is greater than that of those with preserved EF.	Rejected
$H_1$1.4: The number of outpatient visits to a cardiologist in HF patients with reduced EF is greater than that of those with preserved EF.	Rejected
$H_1$1.5: The number of emergency department visits in HF patients with reduced EF is greater than that of those with preserved EF.	Rejected
Objective 2 To determine whether healthcare costs differ between HF patients with reduced and preserved EF.	
$H_1$2.1: The prescription costs of HF patients with reduced EF will be higher than in those with preserved EF.	Rejected

Table 3.30: Results of Hypotheses Testing (continued)

Objectives and Alternate Hypotheses (H_1)	Result
$H_1$2.2: The inpatient costs of HF patients with reduced EF will be higher than in those with preserved EF.	Rejected
$H_1$2.3: The outpatient costs of HF patients with reduced EF will be higher than in those with preserved EF.	Rejected
$H_1$2.4: The total overall costs of HF patients with reduced EF will be higher than in those with preserved EF.	Rejected
Objective 3 To determine whether prevalence of comorbidities differ between HF patients with reduced and preserved EF.	
$H_1$3.1: The prevalence of diabetes in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.2: The prevalence of dyslipidemia in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.3: The prevalence of hypertension in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.4: The prevalence of coronary heart disease in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Failed to reject
$H_1$3.5: The prevalence of cardiomyopathy in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Failed to reject
$H_1$3.6: The prevalence of dysrhythmia in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.7: The prevalence of valvular heart disease in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.8: The prevalence of depression in HF patients with preserved EF will be significantly higher than in those with reduced EF.	Failed to reject
$H_1$3.9: The prevalence of tobacco use in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$3.10: The prevalence of alcohol/other drug use in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected

Table 3.30: Results of Hypotheses Testing (continued)

Objectives and Alternate Hypotheses (H_1)	Result
Objective 4 To determine whether medication use differs differ between HF patients with reduced and preserved EF.	
$H_1$4.1: The use of anticoagulants in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$4.2: The use of antiarrhythmics in HF patients with reduced EF will be significantly lower than in those with preserved EF.	Rejected
$H_1$4.3: The use of antilipemics in HF patients with reduced EF will be significantly lower than in those with preserved EF.	Rejected
$H_1$4.4: The use of cardiotonics in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$4.5: The use of beta-blockers in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$4.6: The use of calcium channel blockers in HF patients with reduced EF will be significantly lower than in those with preserved EF.	Failed to reject
$H_1$4.7: The use of RAAS-inhibiting agents in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$4.8: The use of diuretics in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected
$H_1$4.9: The number of unique drugs used in HF patients with reduced EF will be significantly higher than in those with preserved EF.	Rejected

EF, ejection fraction; and RAAS, renin-angiotensin-aldosterone system.

Chapter 4: Discussion and Conclusion

Discussion

The purpose of this study was to assess differences in healthcare resource utilization and associated costs between HF patients with reduced versus preserved EF. It also sought to describe differences in medication use and prevalence of comorbidities between the two groups. Although a greater proportion (70%) of the HF patients in this study had a preserved EF compared to about 50% as described in the literature,[10,25-27] our findings support current evidence that those with a preserved EF are more likely to be female and older compared to the group with reduced EF.[9,11,14]

EF measurements are important in classifying HF patients due to differences in patient demographics, comorbidities, and response to therapies; thus it is recommended by the ACCF/AHA guidelines to obtain an EF measurement in patients who have had a significant change in clinical status, such as a hospitalization. However, this study found that only 56% of patients had an EF measurement within 1 month of the index HF admission, with an average lag time between EF measurement and HF admission of about 3.8 months. Owan et al found that 76% of patients had an EF measurement within 1 month of an HF hospitalization,[10] and a more recent study in patients at Kaiser Permanente found that only 34% of hospitalized HF patients had an echocardiogram and EF measurement during a HF admission.[64] There seems to be a common trend of a large proportion of HF admissions lacking an associated EF measurement in retrospective database analyses. This reveals the potential for suboptimal practices, such as not ordering or documenting results of an echocardiogram for a hospitalized HF patient, or miscoding the principal diagnosis for admission.

In terms of healthcare resource utilization, results of this study showed that HF patients with preserved EF had significantly more primary care visits, but fewer cardiology visits, than those with reduced EF. These findings support those of Nichols et al., which found that HF patients with preserved EF incurred significantly more annualized outpatient visits and emergency room visits than those with reduced EF, despite small absolute differences.[64] Inpatient and pharmacy utilization did not differ in either study.

Hospitalizations are common after an HF diagnosis. A study in Minnesota showed that 4 out of 5 HF patients were hospitalized at least once, with over 40% hospitalized more than 4 times throughout the study period.[57] Desai et al. found that among 60% of HF patients who were hospitalized, those with a reduced EF had higher rates of cardiovascular-related hospitalization compared to those with a preserved EF.[65] This study found that a vast majority (94%) of all patients had at least 1 re-hospitalization in the year following the index admission, with 25% having 5 or more hospitalizations. In support of existing literature, our findings suggest that although re-hospitalizations are common among HF patients, the patients' EF has little impact on inpatient or pharmacy resource utilization in the year after an HF hospitalization. However, those with preserved EF seem to have more primary care visits and fewer cardiology-related encounters than those with reduced EF.

We found that costs following a HF hospitalization, including inpatient, outpatient, pharmacy, and total costs, did not differ between the two groups, with total 1-year mean costs of about $12,000 after the index event. Similarly, the NHLBI Cardiovascular Health Study in 2006 found that 5-year overall costs were similar between those with reduced versus preserved EF, ranging from $32,000 to $49,000, despite reduced EF patients having more cardiology visits

and cardiac procedures.[56] However, the previously mentioned study did not stratify cost differences by healthcare segment (i.e., inpatient, outpatient, pharmacy, etc).

This study found that HF patients with preserved EF had a higher prevalence of depression, and those with reduced EF had a higher prevalence of coronary heart disease and cardiomyopathy. The latter two support the fact that these are common etiologies of HF, as well as earlier findings that HF with reduced EF is associated with more coronary heart disease.[10] Also, at 62%, we found that the prevalence of coronary heart disease in those with preserved ejection fraction was higher than what was previously reported, ranging from 36% to 53% in the literature.[56,64]

Previously, studies have identified differences in other comorbidities between the two groups. For example, Steinberg et al showed that HF with preserved EF is associated with greater prevalence of hypertension, obesity, atrial fibrillation, diabetes, and anemia compared to those with reduced EF,[11,15] and another study showed that HF patients with preserved EF had a higher risk of noncardiovascular death in comparison to those with reduced EF.[22] These differences in comorbidities further highlight distinctive features between both groups, especially since guideline-recommended therapies of those with preserved EF are focused on treatment of comorbid conditions rather than the HF itself.[12]

At baseline, a greater proportion of HF patients with reduced EF had antiarrhythmic use, while those with preserved EF had more use of calcium channel blockers. After adjusting for covariates, we found that HF with reduced EF remained predictive of less calcium channel blocker use after a HF hospitalization. This is not surprising, as clinical guidelines do not recommend routine use of calcium channel–blocking agents in HF with reduced EF.[12] In

contrast, a Cardiovascular Research Network study found that HF patients with reduced EF were less likely to be treated with cardiac and HF therapies prior to their index HF event; however they were significantly more likely to be treated with new cardiac medications and HF therapies after their HF diagnosis compared to those with preserved EF.[66]

Limitations

This study has several limitations. Retrospective analyses using claims data and electronic medical records may not include complete patient information and rationale behind clinical management of patients. In addition, prescription fills obtained via pharmacy claims only indicate that a patient picked up the medication, but does not confirm whether the patient has actually taken it. Comorbidities were obtained from diagnosis codes in medical claims, consequently were likely to be underestimated. Several HF index admissions did not have a recent EF measurement, thus placement of these patients in either study group was based on an outdated EF measurement. The small sample size of the study and the fact that not all subjects had a full two years of data also limit the interpretation of the results. Due to the chronic nature of HF and its associated long term sequelae, the 1-year follow-up period may not have provided adequate insight to long term outcomes and costs. Finally, the patient population is predominantly in rural Central Texas and may differ from the rest of Texas and the US, thereby potentially limiting the generalizability of the study.

Conclusion

As novel and costly therapies for HF are on the horizon, it is important to understand differences in healthcare utilization between patients with reduced versus preserved EF to

make informed decisions about allocation of resources. This study demonstrated that healthcare utilization and associated costs are similar between HF patients with reduced and preserved EF, thus HF can be considered a single entity in terms of overall resource use. We also found that HF patients with reduced EF have higher prevalence of coronary heart disease and cardiomyopathy and less use of calcium channel blockers. Results of this study also suggest a need for improvement in obtaining an echocardiogram and EF measurement during an HF hospitalization, as recommended by clinical guidelines. Further research is needed to evaluate other outcomes, including potential differences in biomarkers such as brain natriuretic peptide, as well as cardiovascular events and mortality. These outcomes should also be assessed over a longer period of time to appropriately capture potential differences occurring in the long term.

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